Journal of Rehabilitation Research and Development
Vol. 40, No. 5, September/October 2003, Supplement 2
Pages 35–44

Effect of ventilation-feedback training on endurance and perceived breathlessness during constant work-rate leg-cycle exercise in patients with COPD

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Abstract—The purpose of this study was to evaluate the efficacy of a unique program of ventilation-feedback training combined with leg-cycle exercise to improve exertional endurance and decrease perceived dyspnea in patients with chronic obstructive pulmonary disease (COPD). Thirty-nine patients (67.5 ± 8.1 yr of age) with moderate to severe COPD (42.6% of predicted forced expiratory volume in 1 s) were randomized to one of three 6-week experimental interventions: ventilation-feedback with exercise (V^{+EX}), exercise only (EX^{ONLY}), or ventilation-feedback only (VF^{ONLY}). At baseline and at 6 weeks, patients completed a constant work-rate leg-cycle ergometer test at 85 percent of maximal power output. There were increases within the groups in exercise duration: 11.5 min (103%), 8.0 min (66%), and 0.4 min (4%) for the VF^{+EX}, EX^{ONLY}, and VF^{ONLY} groups, respectively. The VF^{ONLY} group experienced no significant within-group changes in selected gas exchange parameters. However, there were significant ($p < 0.05$) posttraining changes in minute ventilation, tidal volume, breathing frequency (f), and expiratory time (Te) in the VF^{+EX} group, and in f and Te in the EX^{ONLY} group. After completing the training, VF^{+EX} and EX^{ONLY} patients reported less breathlessness and perceived exertion ($p < 0.05$). The VF^{ONLY} patients' ratings changed in the hypothesized direction but were not significant. Based on these preliminary data, VF^{+EX} and EX^{ONLY} were equally effective in improving leg-cycle exercise tolerance in patients with moderate to severe COPD.

Key words: exercise, chronic obstructive pulmonary disease (COPD), pulmonary rehabilitation.

INTRODUCTION

The term chronic obstructive pulmonary disease (COPD) is used to characterize those individuals with chronic bronchitis or emphysema who have obstruction to airflow on a spirogram [1]. Individuals with COPD have a poor exercise capacity that is reflective of their underlying disease [2]. Goals of pulmonary rehabilitation include alleviating dyspnea and improving physical activity tolerance. Dynamic hyperinflation contributes to the perception of dyspnea and reduced exercise tolerance [3]. In the presence of dynamic hyperinflation, the end-expiratory

Abbreviations: AUC = area under the curve, BP = blood pressure, COPD = chronic obstructive pulmonary disease, CWR = constant work rate, ECG = electrocardiograph, HR = heart rate, IC = inspiratory capacity, MMSE = Mini-Mental Status Exam, RPB = rating of perceived breathlessness, RPE = rating of perceived exertion, VE = minute ventilation, VT = tidal volume.

This material was based on work supported by the Department of Veterans Affairs, Veterans Health Administration, Rehabilitation Research and Development Service, Proposal F2302-R and Career Development Award D1003CD.

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lung volume increases and the tidal volume (VT) response to exercise is truncated [3]. As a result, the inspiratory muscles must generate increased pressure for inspiratory flow to begin. In an attempt to control increases in end-expiratory lung volume during exercise, we developed a computerized ventilation-feedback program. In this study, ventilation-feedback refers to the visual and auditory presentation of a simple indicator of inhalation and exhalation (moving horizontal bar), and a display to designate a subject's successful or unsuccessful effort to satisfy the investigator's preset breathing pattern parameters. We designed the ventilation-feedback system to train patients to prolong expiratory time and maintain VT during exercise.

It was hypothesized that individuals with COPD who completed a 6-week program of ventilation-feedback training combined with a moderately high-intensity leg-cycle exercise and upper body strength training would demonstrate significantly longer exercise duration, less hyperinflation, and a lower perception of breathlessness and rating of perceived exertion during a constant work rate (CWR) leg-cycle exercise test when compared to subjects who were randomly assigned to either a moderately high-intensity leg-cycle exercise and upper body strength training program or ventilation-feedback training only program.

METHODS

Subject Selection and Screening

All volunteers were given a verbal and written explanation of the purpose, procedures, and potential risks of participation in the research. Written informed consent was obtained from all subjects. Study inclusion criteria were partial pressure of arterial oxygen ≥56 mmHg at rest; a mean percent oxygen saturation (SpO_2) ≥85 percent at peak exercise (with or without supplemental O_2); a forced exhalation in 1 s/forced vital capacity ratio (FEV_1/FVC) ≤70 percent; normal blood urea nitrogen and albumin (nonmalnourished); and no respiratory infection in the previous 4 weeks. Subjects were screened for reversibility.

Subjects

Forty-seven subjects were enrolled in the study; data are reported on 39 subjects that completed the 6 weeks of training. Eight patients withdrew from the study after completing or partially completing baseline testing. Two of these individuals had been randomized (both to the exercise only group) and left the study because of an unrelated illness. Subjects' reasons for withdrawing or being withdrawn included "not interested" (n = 2), "time commitment too great" (n = 1), noncompliance with baseline testing (n = 1), claudication (n = 1), and coronary artery disease (n = 1). No significant differences in demographic characteristics were found between those that were dropped from the study and those who completed 6 weeks of training. At baseline, the three experimental groups were not significantly different from each other on any of the demographic characteristics listed in **Table 1** ($p > 0.05$). None of the subjects were found to have reversible disease.

PROCEDURES

Screening and Baseline Testing

All candidates underwent a physical examination, a pulmonary function test, and an arterial blood gas test. Participants completed a symptom-limited leg-cycle ergometer test and two CWR leg-cycle ergometer tests at a workload equal to 85 percent of the maximal power output achieved on the symptom-limited leg-cycle exercise test with metabolic measurements. All exercise tests were separated by a minimum of 48 hr. If the difference in exercise duration was greater than 10 percent, a third test was completed. After finishing all baseline testing, subjects were randomized into one of three experimental conditions: exercise (leg-cycle training) + ventilation-feedback (VF^{+EX}), exercise only (EX^{ONLY}), or ventilation-feedback only (VF^{ONLY}).

Exercise Prescription

An individualized interval training exercise prescription was prepared for each participant in the two exercise groups. The exercise prescription specified exercise intensity, duration of exercise interval, length of recovery interval, and number of repetitions. Sixty-five to seventy-five percent of each training session included exercise at an intensity of 80 to 85 percent of peak oxygen uptake (VO_{2peak}). Every training session included one or two sets of progressive resistance upper body exercise using elastic bands or dumb bells. All subjects were expected to exercise three times per week for approximately 30 to 50 min (time does not include recovery intervals).

Table 1.
Sample demographics (mean ± 1 standard deviation) and peak metabolic and hemodynamic measurements from baseline symptom-limited progressive leg-cycle exercise test partitioned by assignment to study experimental conditions: ventilation-feedback with exercise (VF^{EX}), exercise only (EX^{ONLY}), and ventilation-feedback only (VF^{ONLY}). Differences between groups were not statistically significant ($p > 0.05$).

Variables	VF^{+EX} ($n = 13$)	EX^{ONLY} ($n = 12$)	VF^{ONLY} ($n = 14$)
Age (yr)	68.9 ± 9.3	65.9 ± 7.6	67.8 ± 7.6
Height (cm)	176.6 ± 5.1	173.4 ± 6.7	174.5 ± 7.7
Weight (kg)	85.7 ± 18.2	78.2 ± 20.4	89.8 ± 22.2
BMI	27.3 ± 4.7	26.1 ± 7.0	29.5 ± 6.9
MMSE	28.5 ± 1.6	28.6 ± 1.1	28.4 ± 1.6
Smoking (Pack yr)	45.9 ± 42.2	63.6 ± 37.3	69.1 ± 68.2
Severity of COPD (GOLD Criteria)			
Moderate (IIa)	$n = 5$	$n = 3$	$n = 8$
Moderate (IIb)	$n = 3$	$n = 5$	$n = 3$
Severe (III)	$n = 5$	$n = 4$	$n = 3$
Pulmonary Function			
FVC (L) [% pred]	2.50 ± 0.93 [62 ± 17]	2.66 ± 0.96 [70 ± 22]	2.68 ± 0.86 [68 ± 20]
FEV_1 (L) [% pred]	1.27 ± 0.72 [40 ± 20]	1.14 ± 0.41 [39 ± 16]	1.43 ± 0.62 [47 ± 18]
FEV_1/FVC [% pred]	48 ± 13 [62 ± 17]	44 ± 13 [56 ± 18]	53 ± 12 [68 ± 16]
Metabolic (Baseline)			
VO_2 ($mL \cdot min^{-1}$)	1245 ± 428	1143 ± 266	1213 ± 295
[% pred]	55 ± 16	49 ± 6	50 ± 10
VCO_2 ($mL \cdot min^{-1}$)	1385 ± 520	1262 ± 294	1194 ± 363
VE ($L \cdot min^{-1}$)	44.3 ± 17.2	37.3 ± 10.9	40.5 ± 12.7
VE/MVV	1.11 ± 0.39	1.00 ± 0.23	0.88 ± 0.23
VT (L)	1.51 ± 0.50	1.28 ± 0.28	1.40 ± 0.48
f ($b \cdot min^{-1}$)	29 ± 4	29 ± 9	30 ± 7
RER	1.03 ± 0.10	1.00 ± 0.09	0.97 ± 0.17
HR ($b \cdot min^{-1}$)	113 ± 17	115 ± 18	111 ± 19
% HR_{MAX}	87 ± 22	87 ± 24	84 ± 28

BMI = body mass index = weight (kg) ÷ height $(m)^2$
MMSE = Mini-Mental Status Exam
FVC = forced vital capacity
FEV_1 = forced expiratory volume in 1 s
[% pred] = percent predicted
VO_2 = oxygen uptake
VCO_2 = carbon dioxide production
VE = minute ventilation
MVV = maximum voluntary ventilation
VT = tidal volume
f = breathing frequency
RER = respiratory exchange ratio
HR = heart rate

Ventilation-Feedback Training

The ventilation-feedback system consisted of a heated Fleish pneumotachometer (Vacumed, Inc.) interfaced to a 486 computer via a 12-bit analog-to-digital converter, enabling measurement of bidirectional airflow. The subject interacted with the system by breathing through a mouthpiece and received visual feedback on the computer monitor.

The feedback screen (see **Figure 1**) was divided in half, with the left portion labeled IN (inhale) and the right labeled OUT (exhale). During expiration, a solid white horizontal bar extended from the centerline toward 1 of 12 round green targets appearing along the right-hand edge of the screen. Similarly, a horizontal bar extended to the left from the centerline during inspiration. The length of each bar increased with the length of time spent in the given respiratory phase. For example, the bar continued to lengthen toward the right as long as the subject continued to exhale. If the expiration phase continued for the requisite length of time, the bar reached the target and the subject scored a “hit.” Alternatively, if expiration was interrupted too soon, the attempt represented a “miss.”

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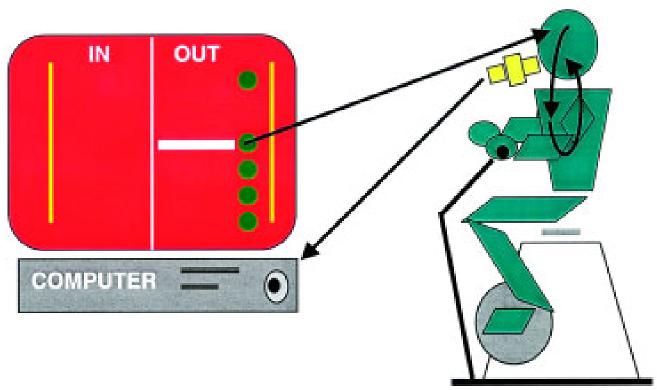

Figure 1.
Illustration of ventilation-feedback screen used by subjects in ventilation-feedback with exercise and ventilation-feedback only groups.

Each hit was accompanied by an audible tone, and a tally of hits and misses was presented on the screen. A performance score was computed at the end of each specified training interval. We have found that with relatively simple instructions, subjects quickly understood and successfully accomplished the feedback task**.**

Duration of expiratory time (Te) required to score a "hit" was specified by the investigator as a multiple of inspiration time (Ti). The initial Te set for training was 10 percent above that recorded at any given workload ($\%VO_2$). Each new target Te was computed from the immediately preceding inspiration or a rolling average of previous Ti. The investigator was also able to set a minimal threshold expiratory flow parameter (L/s). The expiratory bar continued to lengthen toward the target only as long as the subject maintained an exhalation flow of air greater than the specified threshold.

Aerobic Fitness and Ventilation-Feedback Training Protocols

Each training session included a 3 min ventilation-feedback practice without exercise (ventilation-feedback groups only), and a 3 to 5 min warm-up, interval training, and cooldown. During every training session, pretraining, training, and posttraining heart rate (HR), blood pressure (BP), and ratings of perceived exertion (RPE) and breathlessness (RPB) were recorded.

Subjects in the EX^{ONLY} group trained at the same intensity as the VF^{+EX} group. While training, EX^{ONLY} subjects underwent the same instrumentation for physiologic measurements as subjects in the ventilation-feedback groups. Subjects in the VF^{ONLY} group trained in ventilation-feedback at rest and with minimal physical activity; i.e., 0 W workload during cycling. The duration of physical activity in the VF^{ONLY} group was limited to 10 min. These exercise workloads were not of sufficient intensity to provide a training effect (<40% of VO_{2peak}) but allowed the individual to practice ventilation-feedback while engaging in physical movement. Workloads were not increased. The VF^{ONLY} participants were presented with the same ventilation-feedback goals as the exercising subjects. Our goal was to set the ventilation-feedback so that the subject's ventilation pattern would parallel the expected physiological adjustments to exercise while controlling the tendency toward dynamic hyperinflation. Preparation of the training prescription for individuals in the ventilation-feedback groups included determination of three elements in addition to those specified above: (a) a performance goal, i.e., the target ventilation-feedback "score"; (b) a target ratio of Te to Ti; (c) a breathing frequency, *f*; and (d) the minimum expiratory air flow. The target ratio of Te to Ti and expiratory airflow were based on the breathing pattern observed during baseline maximal exercise tests. The initial ventilation-feedback training Te/Ti, *f*, and flow were based on the values measured at rest, 40, 60, 70, 80, and 90 percent of the VO_{2peak} achieved during the baseline exercise test. When the subject was able to exercise at 85 percent of VO_{2peak} with a "feedback score" >85 percent, the settings were raised by ~5 percent.

After each conditioning session on the leg-cycle, subjects completed an upper body muscle endurance/strength training session. The progressive resistance muscle endurance/strength-training program involved the use of rubber bands (TheraBand™ and dumb bells). Participants performed upper body exercises that employed the accessory muscles of respiration. The training included six to eight exercises (e.g., tricep extensions, lateral arm raises), was progressive (i.e., bands with greater resistance and heavier weights were used as participants strength increased), and was completed in one to two sets of 12 to 15 repetitions per exercise. Upper body progressive resistance training was included because tasks performed with the arms have generally been associated with increased perceived dyspnea in patients with COPD [3].

Exercise Testing Protocols

Symptom-Limited Leg-Cycle Ergometer Test Protocol

An electrically braked bicycle ergometer was used (Corival 400, Quinton Instrument Company, Seattle, WA), and, in preparation for testing, the seat height adjusted. Before mounting the leg-cycle ergometer, the subject completed a preexercise flow volume loop and slow vital capacity test. The first stage of the continuous protocol was 2 min of unloaded pedaling at 60 rev-min^{-1}. Subsequent stages were 2 min long, with power output increases of 10 W per stage. All maximal symptom-limited exercise tests were supervised by a physician, clinical nurse specialist, and/or trained technician.

Constant Work-Rate Submaximal Leg-Cycle Ergometer Protocol

After 2 min of unloaded cycling, subjects exercised on the electrically braked ergometer at a workload at which they reached 85 percent of their VO_{2peak} on the symptom-limited, maximal leg-cycle exercise test.

For all exercise tests, subjects exercised until they were (a) unable to maintain the designated work intensity, (b) were exhausted and unable to continue, (c) had significant signs or symptoms develop, or (d) experienced unusual or severe shortness of breath. Exercise tests were separated by a period of 48 hr and conducted at the same time of day. The same instructions were given to patients at baseline and after 6 weeks of training.

Measurements

Oxygen uptake (O_2, mL•min^{-1}) was determined using a MedGraphics CPX/MAX/D^{TM} System (MedGraphics Corp., St. Paul, MN). Breath-by-breath measures were averaged in 30 s intervals. Before each test, the analyzers were calibrated with reference gases and room air. For subjects who became hypoxemic with exercise, an oxygen reservoir system (Douglas bag technique, 60 L) was used to supply continuous 30 percent O_2.

Minute ventilation (VE), VT, and *f* were determined with the MedGraphics Metabolic Measurement Cart mass flowmeter. Volume, barometric pressure, and temperature calibrations were completed before each exercise test.

Inspiratory Capacity

Inspiratory capacity (IC) was measured 60 s before beginning exercise, at the end of every stage, within 30 s of the end of exercise, and at 2 and 4 min of recovery.

Heart rate was derived from a standard electrocardiograph (ECG). A MedGraphic CardioPerfect ECG was used for continuous visual monitoring (leads II, V1, and V5) and recording. A 12 lead ECG was taken every minute during all exercise tests.

Blood pressure was measured before exercise, every 2 min while the subject was exercising, and every minute after exercise, until the patient's BP approached baseline values.

Ratings of perceived breathlessness and exertion were obtained using Borg's ratio scale [4,5]. Ratings were taken during the last 30 s of each stage of exercise. Ratings of perceived breathlessness and exertion ranged from 0 (no breathlessness/exertion) to 10 (maximal breathlessness/exertion). The Borg scale has been widely used and has established validity and reliability [6,7].

Mini-Mental Status Exam (MMSE)

Cognitive ability may influence an individual's understanding and mastery of the ventilation-feedback technique. The MMSE was used to measure cognitive function at baseline. Reliability and validity of the MMSE have been empirically established [8]. Subjects with a score ≤23 (some degree of cognitive impairment) were excluded from the study.

Data Analysis

Descriptive statistics were used to summarize baseline characteristics of the study sample and changes in outcome measures from baseline to end of treatment. Statistical comparisons were carried out on all baseline variables to determine whether any imbalances on important prognostic factors existed. Specifically, baseline functional status (i.e., duration on the progressive and CWR cycle tests and the pulmonary function parameters), were compared across the three groups. All tests were two-sided and were considered significant at $p < 0.05$.

The Kruskal-Wallis test was used as an omnibus test of differences between groups. Within-group differences were determined using the Wilcoxon sign-rank test for paired samples.

Changes in duration and selected gas exchange parameters on the CWR leg-cycle ergometer test were computed for baseline and 6 weeks. A Wilcoxon sign-rank test, using change scores, was used to compute the differences within the groups from baseline to 6 weeks. Ventilatory parameters were compared at an isotime, determined with the 30 s average of breath-by-breath data during the last 2 min of exercise on the baseline test. Data at 6 weeks were compared at this same point in that exercise test.

Slopes for the relationship between RPB and exercise stage and RPE and exercise stage during the CWR exercise test were determined for each participant with linear regression. The slope and the intercept of the dyspnea rating were recorded. The change in slope was computed for each individual subject (Δ slope = slope$_{baseline}$ – slope$_{6\ wk}$). Changes in RPB and RPE slopes and intercepts were compared using Wilcoxon sign-rank test.

The areas under the curves for RPB (AUC_{RPB}) and RPE (AUC_{RPE}) were derived from plots of individual subjects' ratings of breathlessness and exertion on exercise time for baseline and 6 week CWR leg-cycle tests. The plots for each individual were limited to an isotime established as the duration of exercise at baseline testing (**Figure 2**). The areas under the curves for RPB and RPE were considered representative measurements of the total dyspnea and exertional burden experienced by the subjects during leg-cycle exercise. It was posited that the area under the curve would decrease following training. The

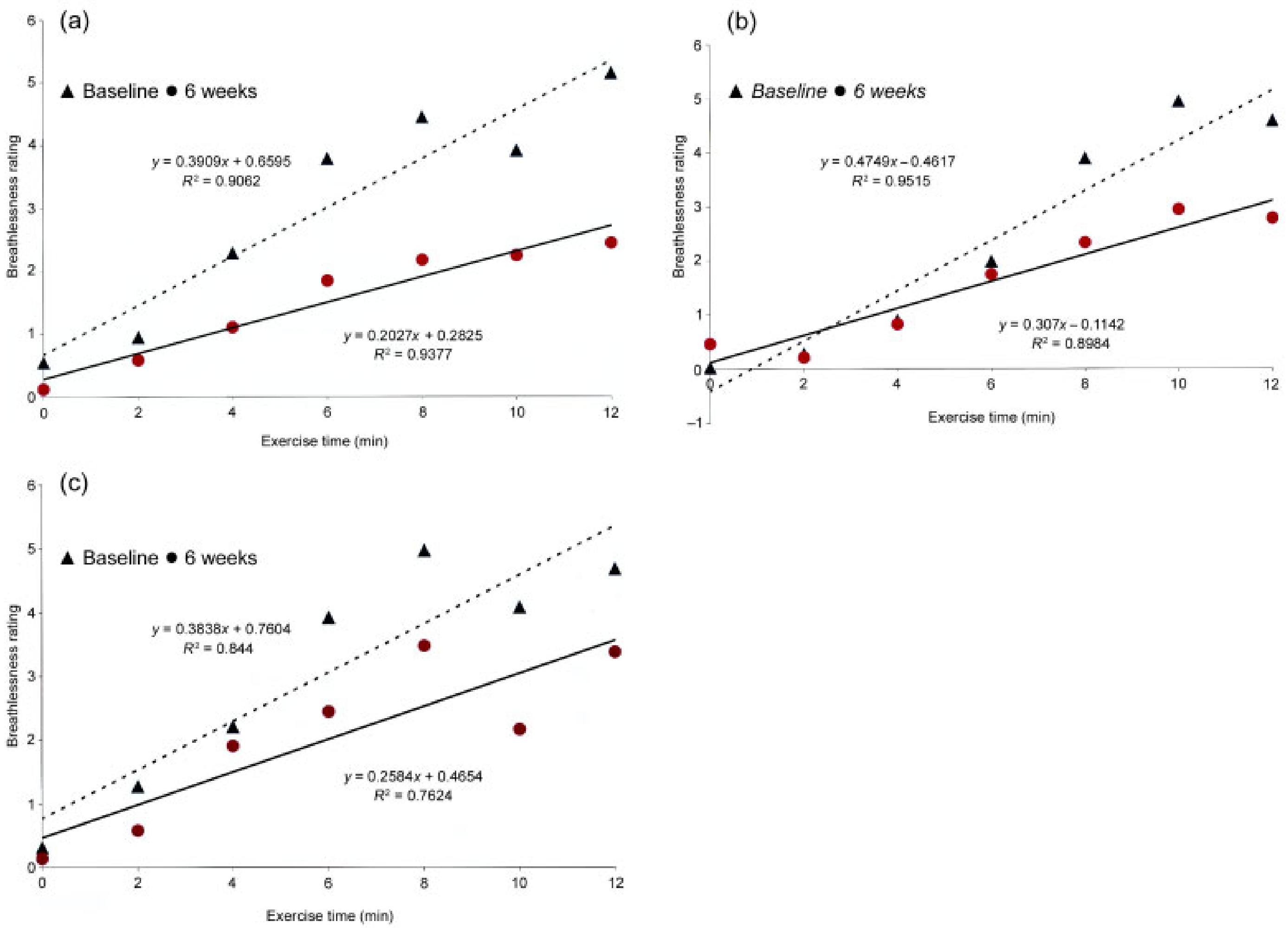

Figure 2.
Three graphs with rating of perceived breathlessness plotted on exercise time at baseline and 6 weeks, and result of linear regression analyses for each experimental group: **(a)** exercise only, **(b)** ventilation-feedback with exercise, and **(c)** ventilation-feedback only. After completing 6 weeks of their respective interventions, patients from all groups showed decrease in slope, indicating that rate of increase in perceived breathlessness during constant work-rate exercise at 85 percent of VO_{2peak} was markedly decreased.

change in the area under the curve was computed for each variable and compared using a Wilcoxon sign-rank test.

The Pearson Product Moment correlation procedure was used to assess the strength of the relationship between selected parameters.

RESULTS

All subjects completed the testing and assigned intervention without complication or injury attributable to study participation. Eighteen training sessions were completed by all subjects. The average subject-investigator contact time was ~60 min per session. All subjects randomized to one of the ventilation-feedback groups were able to successfully complete ventilation-feedback training. This was evidenced by the percentage of “hit” scores ranging from 60 to 100 percent on the first day of training.

The only significant difference between groups was in the change in exercise duration between baseline and 6 weeks. The change in the cycling time at 6 weeks was significantly less in the VF^{ONLY} than in the VF^{+EX} ($p < 0.003$) group. There was no significant difference in exercise endurance between the VF^{+EX} and EX^{ONLY} groups. In order to achieve statistical significance (80% power, $\alpha = 0.05$) between the VF^{+EX} and EX^{ONLY} groups, 85 subjects would be needed in each group. There was a within-group increase in exercise duration 11.5 min (103%), 8.0 min (66%), and 0.4 min (4%) for the VF^{+EX}, EX^{ONLY} and VF^{ONLY} groups, respectively (**Figure 3**). Data from the CWR leg-cycle testing used for statistical comparisons was taken at an isotime established as the last 30 s of the final stage of exercise completed by a subject during baseline testing. All between-group comparisons of changes in gas exchange variables between baseline and 6 weeks were nonsignificant ($p > 0.05$). The VF^{+EX} group produced the greatest number of significant within-group changes from baseline to 6 weeks (**Table 2**). In addition to an increase in exercise duration, HR ($p = 0.047$), VE ($p > 0.0001$), f ($p = 0.01$), and RPB ($p = 0.003$) were lower, and Te ($p = 0.04$) was higher. The exercise-only group showed similar improvements after completing the 6 week intervention, with the exceptions of a decrease in RPE ($p = 0.05$) and a nonsignificant increase in Te and decrease in VE. There were no changes observed in the VF^{ONLY} group.

The calculated AUC_{RPE} and AUC_{RPB} decreased in the VF^{+EX} ($p = 0.04$ and 0.03) and EX^{ONLY} ($p = 0.004$ and 0.012) following completion of their respective interventions (**Table 3**, **Figure 4**). The AUC_{RPE} and AUC_{RPB} values also decreased in the VF^{ONLY} group, but failed to reach statistical significance ($p = 0.096$ and 0.136). The EX^{ONLY} group alone exhibited a decrease in the slope for RPE ($p = 0.018$) and RPB ($p = 0.016$) plotted on exercise time. However, there was a decrease in slope for all the experimental groups (**Figure 2**). This suggests that, regardless of study group assignment, subjects experienced, while leg cycling at 85 percent of baseline VO_{2peak}, a lower rate of increase in RPE up to an investigator-established isotime (see above).

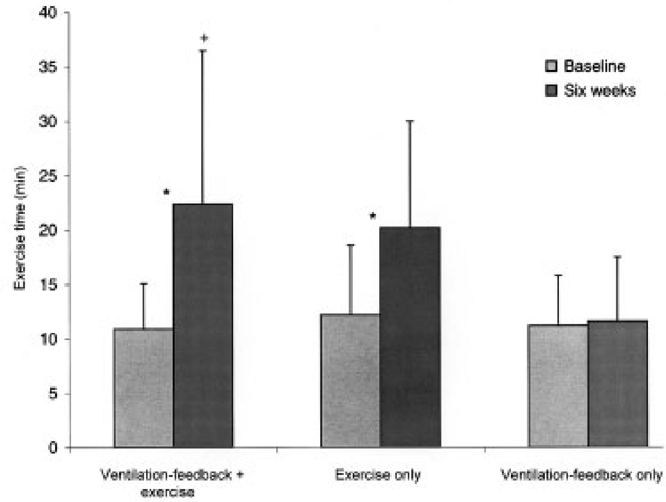

Figure 3.
A histogram presentation of the exercise duration (mean ± 1 standard deviation) on constant work-rate leg-cycle ergometer exercise tests at baseline and following 6 weeks of intervention for the ventilation-feedback plus-exercise, exercise-only, and ventilation-feedback-only experimental groups. Within-group changes from baseline to 6 weeks for ventilation-feedback with exercise and exercise-only groups were significant (*). Between-group change for ventilation-feedback with exercise and ventilation-feedback only was significant (+).

In the VF^{+EX} group, a Pearson Product Moment correlation analysis revealed a negative relationship ($r = -0.68$, $p = 0.04$) between the change in IC measured during the initial and 6 week CWR leg-cycle test ($\Delta = IC^{6wk} - IC^{Baseline}$) and change in the AUC_{RPB}.

DISCUSSION

The findings in this preliminary report were that (a) subjects assigned to the VF^{+EX} group improved their exercise tolerance significantly more than those assigned

Table 2.
Comparison of selected measurements (mean ± 1 standard deviation) from baseline and 6-week constant work-rate leg-cycle exercise test at isotime (see text) partitioned by experimental conditions: ventilation-feedback with exercise (n = 13), exercise only (n = 12), and ventilation-feedback only (n = 14).

Measurements	Ventilation-Feedback Plus Exercise		Exercise Only		Ventilation-Feedback Only	
	Baseline	6 Weeks	Baseline	6 Weeks	Baseline	6 Weeks
HR ($b \cdot min^{-1}$)	120 ± 23	114 ± 19*	119 ± 13	112 ± 10*	108 ± 14	108 ± 16
SpO_2 (%)	95.3 ± 1.4	96.0 ± 2.5	94.2 ± 3.5	95.1 ± 2.8	95.4 ± 2.3	95.6 ± 2.7
VO_2 ($mL \cdot min^{-1}$)	1296 ± 452	1267 ± 456	1157 ± 253	1131 ± 252	1118 ± 357	1065 ± 332
CO_2 ($mL \cdot min^{-1}$)	1272 ± 505	1214 ± 460	1195 ± 355	1135 ± 281	1029 ± 451	1010 ± 417
VE ($L \cdot min^{-1}$)	45.5 ± 17.7	41.6 ± 15.6*	39.9 ± 12.2	37.2 ± 10.7	37.8 ± 13.4	37.2 ± 37.2
VT ($L \cdot min^{-1}$)	1.6 ± 0.5	1.7 ± 0.6	1.3 ± 0.3	1.3 ± 0.3	1.3 ± 0.4	1.5 ± 0.6
f ($b \cdot min^{-1}$)	28 ± 4	26 ± 3*	32 ± 1	29 ± 8*	28 ± 6	27 ± 8
Ti (s)	0.72 ± 0.23	0.77 ± 0.16	0.65 ± 0.19	0.70 ± 0.19	0.69 ± 0.20	0.75 ± 0.19
Ti/T_{TOT}	0.33 ± 0.09	0.33 ± 0.07	0.33 ± 0.04	0.32 ± 0.05	0.33 ± 0.05	0.34 ± 0.06
Te (s)	1.42 ± 0.29	1.56 ± 0.30*	1.34 ± 0.38	1.46 ± 0.39	1.41 ± 0.32	1.56. ± 0.57
RPE	5.3 ± 3.5	3.7 ± 3.5	5.6 ± 3.7	2.4 ± 2.0*	5.5 ± 3.6	3.9 ± 3.4
RPB	5.2 ± 3.3	3.2 ± 3.2*	5.9 ± 3.8	2.7 ± 2.2*	5.1 ± 3.7	3.6 ± 3.4
IC (L)	2.2 ± 0.7	2.5 ± 0.8*	2.0 ± 0.7	1.9 ± 0.7	2.0 ± 0.5	2.1 ± 0.8

*Significant ($p < 0.05$) within-group differences
HR = heart rate
SpO_2 = oxyhemoglobin saturation (pulse oximetry)
VO_2 = oxygen uptake
CO_2 = carbon dioxide production
VE = minute ventilation
VT = tidal volume
f = breathing frequency
Ti = inhalation time
Ti/T_{TOT} = ratio inspiratory time to duty cycle (Ti + Te)
Te = exhalation time
RPE = rating of perceived exertion
RPB = rating of perceived breathlessness
IC = inspiratory capacity

Table 3.
Within-group analyses of area under curve for rating of perceived exertion (AUC_{RPE}) and perceived breathlessness (AUC_{RPB}) during progressive, symptom-limited leg-cycle exercise tests at baseline and 6 weeks.

Group	AUC_{RPE}		p	AUC_{RPB}		p
	Baseline	6 Weeks		Baseline	6 Weeks	
VF with Exercise	134 ± 123	88 ± 98	0.04	127 ± 118	87 ± 102	0.03
Exercise Only	182 ± 190	85 ± 98	0.004	188 ± 198	88 ± 90	0.012
VF Only	119 ± 94	89 ± 105	0.096	127 ± 106	90 ± 110	0.136

VF = ventilation-feedback

to the VF^{ONLY} group; and (b) all groups reported significantly less dyspnea after 6 weeks of ventilation-feedback and/or exercise training.

Exercise duration on the CWR submaximal leg-cycle ergometer protocol improved significantly from baseline to 6 weeks in the VF^{+EX} and EX^{ONLY} groups, but not in the VF^{ONLY} group. Subjects randomized to VF^{+EX} group performed significantly better than the VF^{ONLY} group. This difference was not surprising, since the VF^{ONLY} group did not complete exercise training. The VF^{ONLY} group did have a 4 percent improvement in overall exercise duration, but this improvement was not significant. This slight improvement in the VF^{ONLY} group may have been attributable to the ventilation-feedback, a small training effect from the 10 min of unloaded cycling, or increased familiarity with the testing conditions.

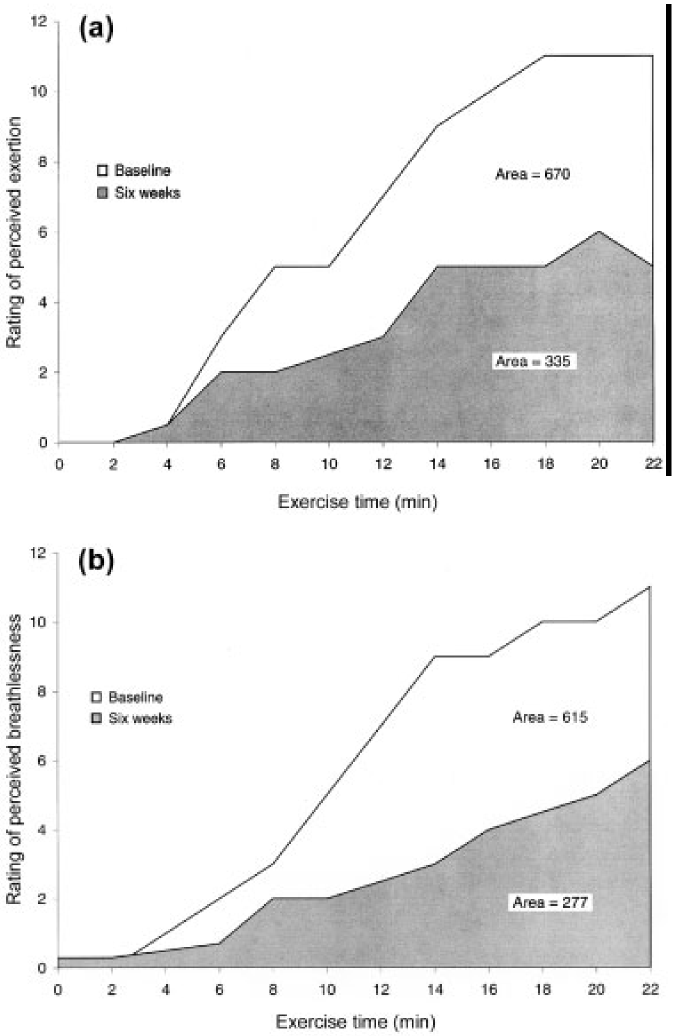

Figure 4.
Plot of data from a representative subject (EX^{ONLY} group) to illustrate the determination of area under the curve that was used to assess differences between baseline and 6-week ratings of **(a)** perceived exertion and **(b)** breathlessness on the constant work- rate leg-cycle exercise test. For this individual, 22 min was maximal duration of exercise during baseline testing. Although subject exercised longer on the 6-week test (21.3 vs. 38.6 min), area under the curve analysis was limited to the maximal exercise time reached during baseline testing. In this way, a fixed isotime for statistical comparison was established.

The VF^{+EX} and EX^{ONLY} groups showed substantive improvements in exercise duration on the CWR test at 6 weeks. Although the between-group difference in the percentage increase in exercise time appears to be relatively large (104 vs. 68%), the substantial within-group variability precluded statistical significance. These increases in exercise duration are equivalent or greater than that previously reported in the COPD literature, as other investigators have reported improvements ranging from 43 to 77 percent [9–11] on CWR leg-cycle ergometer tests. Direct comparisons between studies are difficult, however, because the CWR exercise tests for the present study were performed at 85 percent of the subjects' VO_{2peak} achieved on the symptom limited progressive leg-cycle exercise test. Others have tested patients at lower exercise intensity. The lower intensity for the CWR test prolongs the test at baseline. Since most CWR tests are capped for duration (i.e., subjects are stopped by the investigator at 45 to 60 min), the percentage of improvement may have been affected in these studies. Additionally, some patients may stop for reasons other than breathlessness or fatigue when an exercise test becomes too prolonged.

Exercise training effects were seen in all the groups, although all parameters were not significant from baseline to 6 weeks. Following the intervention, HR was lower at isotime in both exercising groups. Oxygen uptake and carbon dioxide production were reduced in all three groups. Although the latter changes have not yet reached within-group significance, there appeared to be a training effect across the three groups.

There was a significant within-group reduction in VE recorded at isotime in the VF^{+EX} group that was not present in the other two groups. This difference was not significant between the groups, but was present within the groups. Although the primary contributor to this reduction in VE was a decrease in frequency, there was a slight increase in VT for the VF^{+EX} and VF^{ONLY} groups. These changes were not seen in the EX^{ONLY} group. There was also a significant, 10 percent increase in Te in the VF^{+EX} group that was not present in the other two groups. To conclude that these changes are due to ventilation-feedback training and not exercise training, we would need more subjects.

In patients with severe COPD, progressive dynamic hyperinflation occurs during exercise and, as a result, increases in VT are limited. Consequently, breathing becomes more tachypneic and a larger fraction of the breath is composed of anatomic dead-space air. Dynamic hyperinflation compromises the inspiratory muscle capacity to generate pressure, and inspiratory muscle weakness results. Casuburi has hypothesized that using slower, deeper breathing with exercise training may increase ventilatory muscle endurance, thereby decreasing dynamic hyperinflation by increasing VT [9].

O'Donnell reported that changes in exertional dyspnea correlated with changes in IC [12]. The present findings show that with V^{+EX}, a decline in breathlessness from baseline to 6 weeks was associated with an increase in IC. Since the total lung capacity does not change during exercise, an increase in IC reflects a smaller end-expiratory lung volume. Subjects in the VF^{+EX} group also demonstrated an expanded VT and prolonged Te, indicating that there may be a reduction in end-expiratory lung volume at isotime. Caution is recommended in the interpretation of this result, because the finding is based on a small sample of subjects. However, if this result should remain unaltered after the addition of more subjects, the merit of adding VF^{+EX} to pulmonary rehabilitation to decrease dynamic hyperinflation in patients with moderate to severe COPD would be supported.

Overall, RPB and RPE analyzed as AUC truncated at the baseline isotime closely approximated each other. There was a significant reduction in the AUC_{RPE} and AUC_{RPB} for the VF^{+EX} and EX^{ONLY} groups. Interestingly, there was also a reduction in breathlessness over time in the VF^{ONLY} group, although this finding was not significant. Another interesting finding was that all groups had similar AUC numbers at 6 weeks, suggesting a similar decrease in perceived dyspnea burden during submaximal exercise testing for all groups. The differences in change scores are the result of the higher scores at baseline in the VF^{+EX} and EX^{ONLY} groups. Although the AUC scores on the baseline test mimics the subject's FEV_1, there was no relationship between the AUC_{RPB} at baseline and the FEV_1 at baseline.

SUMMARY

One of the principle goals of pulmonary rehabilitation is to reduce symptoms. An important finding of the present study was that all groups, as illustrated by regression and AUC analyses, experienced a reduction in symptoms of dyspnea. All subjects are continuing in a contiguous 6 week treadmill exercise program. The additional training time may serve to differentiate between the two interventions. The possibility of a Type II statistical error as the primary cause of the nonsignificant difference between these two groups cannot be ignored. At present, it can only be concluded that VF^{+EX} and EX^{ONLY} are equally effective in improving leg-cycle exercise tolerance in patients with COPD.

ACKNOWLEDGMENTS

We are grateful to the Pulmonary Function Laboratory staff for making time to fit our subjects into their busy clinical testing schedule. We thank Terrya Miller and Desi Avila for their help with subject screening, training, and testing; and Dr. S. Kumar for her gracious and generous assistance in providing physician supervision for numerous maximal exercise tests. To the veterans who volunteered and unselfishly made good on their commitment to complete this demanding study, we extend our sincere appreciation.

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Submitted for publication January 20, 2003. Accepted in revised form June 17, 2003.